CLAIMS

We claim:

1. A targeting construct comprising:

   (a) a first polynucleotide sequence homologous to at least a first portion of an ACTHR gene;

   (b) a second polynucleotide sequence homologous to at least a second portion of the ACTHR gene; and

   (c) a selectable marker.

2. A method of producing a targeting construct, the method comprising:

   (a) providing a first polynucleotide sequence homologous to at least a first portion of an ACTHR gene;

   (b) providing a second polynucleotide sequence homologous to at least a second portion of the ACTHR gene;

   (c) providing a selectable marker; and

   (d) inserting the first sequence, second sequence, and selectable marker into a vector, to produce the targeting construct.

3. A cell comprising a disruption in an ACTHR gene.

4. The cell of claim 3, wherein the cell is a murine cell.

5. The cell of claim 4, wherein the murine cell is an embryonic stem cell.

6. A non-human transgenic animal comprising a disruption in an ACTHR gene.

7. The non-human transgenic animal of claim 6, wherein the transgenic animal is a mouse.

8. A cell derived from the transgenic mouse of claim 7.

9. A method of producing a transgenic mouse comprising a disruption in an ACTHR gene, the method comprising:

   (a) introducing the targeting construct of claim 1 into a cell;

   (b) introducing the cell into a blastocyst;

   (c) implanting the resulting blastocyst into a pseudopregnant mouse, wherein said pseudopregnant mouse gives birth to a chimeric mouse; and

   (d) breeding the chimeric mouse to produce the transgenic mouse.

10. A method of identifying an agent that modulates the expression or function of an ACTHR gene, the method comprising:

    (a) providing a non-human transgenic animal comprising a disruption in an ACTHR gene;

    (b) administering an agent to the non-human transgenic animal; and

    (c) determining whether the expression or function of the disrupted ACTHR gene in the non-human transgenic animal is modulated.

11. A method of identifying an agent that modulates the expression or function of an ACTHR gene, the method comprising:

    (a) providing a cell comprising a disruption in an ACTHR gene;

    (b) contacting the cell with the agent; and

    (c) determining whether the expression or function of the ACTHR gene is modulated.

12. The method of claim 11, wherein the cell is derived from the non-human transgenic animal of claim 6.

13. An agent identified by the method of claim 10 or claim 11.

14. A transgenic mouse comprising a disruption in an ACTHR gene, wherein there is no significant expression of the ACTHR gene in the transgenic mouse.

15. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits an adrenal gland abnormality.

16. The transgenic mouse of claim 15, wherein the adrenal gland abnormality comprises adrenal gland hypoplasia.

17. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits decreased cytoplasmic lipid vacuolation in brown adipose tissue, relative to a wild-type mouse.

18. A transgenic mouse comprising a disruption in an ACTHR gene, wherein the transgenic mouse exhibits an adipose tissue abnormality, relative to a wild-type mouse.

19. The transgenic mouse of claim 18, wherein the adipose tissue abnormality is characterized by reduced body fat percentage in the transgenic mouse, relative to a wild-type mouse.

20. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits a metabolic abnormality.

21. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits increased susceptibility to seizure.

22. The transgenic mouse of claim 21, wherein the mouse exhibits seizure-like responses at a lower dose of Metrazol, relative to a wild-type mouse.

23. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits increased activity relative to a wild-type mouse.

24. The transgenic mouse of claim 23, wherein the transgenic mouse is hyperactive.

25. The transgenic mouse of claim 24, wherein the hyperactivity is characterized by increased distance traveled in an open field test, relative to a wild-type mouse.

26. A transgenic mouse comprising a homozygous disruption in an ACTHR gene, wherein the transgenic mouse exhibits anti-depressive behavior, relative to a wild-type mouse.

27. The transgenic mouse of claim 26, wherein the transgenic mouse exhibits reduced time immobile when tail-suspended.

28. A cell derived from the transgenic mouse of claim 14.

29. A method of identifying an agent that ameliorates a phenotype associated with a disruption in an ACTHR gene, the method comprising:

    (a) administering an agent to a transgenic mouse comprising a disruption in an ACTHR gene; and

    (b) determining whether the agent ameliorates at least one of the following phenotypes: an adrenal gland abnormality, an adipose tissue abnormality, a metabolic abnormality, increased activity, anti-depressive behavior, or increased susceptibility to seizure.

30. An agent identified by the method of claim 29

31. A method of treating susceptibility to seizure, the method comprising administering to a subject in need a therapeutically effective amount of ACTHR.

32. A method of treating hyperactivity, the method comprising administering to a subject in need a therapeutically effective amount of ACTHR.

33. A pharmaceutical composition comprising an ACTHR protein.

34. A method of identifying an agent that ameliorates susceptibility to seizure, the method comprising:

(a) administering a putative agent to the transgenic mouse of claim 21; and

(b) determining whether the agent has an affect on susceptibility to seizure in the transgenic mouse.

35. A method of identifying an agent that ameliorates hyperactivity, the method comprising:

(a) administering a putative agent to the transgenic mouse of claim 23; and

(b) determining whether the agent has an affect on hyperactivity in the transgenic mouse.

36. A method of identifying an agent that inhibits the activity or function of ACTHR, the method comprising:

(a) providing a cell expressing ACTHR;

(b) contacting the cell with an agent; and

(c) determining whether the agent inhibits the activity or function of ACTHR, wherein the agent has an affect on depression.

37. An agonist or antagonist of ACTHR.

38. Phenotypic data associated with a transgenic mouse comprising a disruption in an ACTHR gene, wherein the phenotypic data is in an electronic database.